ATTACHMENT A

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT APPLICATION OF Moriarty, R.M.; Penmasta, R.; Guo, L.; Rao, M.S.; and Mehta, R.G.	)	
SERIAL NO.: 09/008,957	)	Group No. 1616
FILED: Jan. 20, 1998	)	Examiner: Badio
TITLE: 1α-HYDROXYVITAMIN D_5, ITS SYNTHESIS AND USE IN CANCER PREVENTION AND THERAPY	)	

DECLARATION UNDER 37 CFR § 1.132

I, Robert M. Moriarty, declare as follows:

1. I am a citizen of the United States residing at 1030 Erie Street, Oak Park, Il 60302.

2. I am a graduate of Fordham University (B.S., 1955) and received a Ph.D. in Chemistry from Princeton University in 1959. I have been conducting research and teaching in a number of areas of organic chemistry for more than 38 years. I have specialized in, among other things, steroids and vitamin D analogs, and started a company ten years ago called Steroids, Ltd., now named SynQuest, Inc., subsidiary of United Therapeutics, Inc.

3. I am currently a professor in the Department of Chemistry at the University of Illinois at Chicago. I am a co-inventor on eight issued US patents on vitamin D analogs, and have authored more than 200 scientific publications in peer reviewed journals.

4. I provided a sample of 1α-Hydroxyvitamin D_5 [1α(OH)D_5] to Dr. Joyce Knutson, Director of Preclinical Research at Lunar Corporation, Madison, WI. Table 1 lists the results of Dr. Knutson's study. The results clearly show that 1α(OH) Vitamin D_5 is considerably less calcemic than its closest known analogs: 1α(OH) Vitamin D_3, 1α(OH)-vitamin D_4 , and 1α,25-$(OH)_2$ Vitamin D_3, all run side-by-side in the same laboratory. This finding is unexpected based on literature precedence, and shows 1α(OH)-vitamin D_5 to be an exciting new and novel compound.

Table I. Effects of Vitamin D analogs on Serum Calcium in Vitamin D-Deficient Rats

Test Compound	Number of rats	Dose (μg/kg/day)	Serum Calcium (mg/100mL) ± S.D.
None (Control)	12	0	5.4 ± 0.28
$1\alpha(OH)D_3$	10	0.042	9.0 ± 1.31
$1\alpha,25(OH)_2D_3$	8	0.042	8.1 ± 1.15
$1\alpha(OH)D_4$	8	0.042	7.1 ± 0.80
$1\alpha(OH)D_5$	8	0.042	**6.0 ± 0.63**
$1\alpha(OH)D_3$	10	0.25	12.0 ± .90
$1\alpha,25(OH)_2D_3$	10	0.25	10.1 ± 1.84
$1\alpha(OH)D_4$	7	0.25	11.6 ± 0.45
$1\alpha(OH)D_5$	10	0.25	**7.9 ± 1.5**

All the data were collected in a single large comparative study at Lunar Corporation, Madison, WI, under the direction of Joyce C. Knutson, Ph.D., Biochemistry (University of Wisconsin), Director of Preclinical Research at Lunar. The methods employed in the study are as follows:

i) The study was conducted using vitamin D deficient weanling rats. Large groups (more than 200 each) of rats were fed a Vitamin D deficient diet (0.47% calcium, 0.3% phosphorous) for three weeks. Animals were then randomly selected from these vitamin D deficient rats and randomly placed into groups for a number of studies, including ours.

ii) The experimental groups were administered doses of test compound at 0.042 and 0.250 mcg/kg/day, with the control group rats receiving a comparable quantity of vehicle, Fractionated Coconut Oil. All doses were administered by gavage once daily for fourteen days.

iii) Animals were observed for clinical signs and mortality once daily. Body weights and food consumption were recorded weekly; the weights varied somewhat at the initiation of the study, and statistically significant increases in mean body weight were observed on Days 7 and 14 in both dose levels of all four test groups when compared with control. Mean food consumption in both dose levels of all four test groups revealed a statistically significant increase when compared with control. No mortality was observed in the animal groups receiving test compounds. At the termination of the study the animals were fasted overnight and blood was withdrawn. Serum calcium determinations were conducted by standard methodology.

5. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of any patent that may issue from the above-identified U. S. patent application.

Robert M. Moriarty

Robert M. Moriarty, Ph.D.

Dec 5, 1999

Date